REMARKS

I. Status of the Claims

Claims 2-5, 7-10, 19-58 and 62 are pending in the application. Claims 1, 6, 11-18, 59 and 60 have been canceled and claims 2-5, 7-10 and 20-58 have been withdrawn pursuant to an election of species. Claims 19 and 62 have been examined and are rejected under 35 USC §101, 35 USC §112, first paragraph, 35 USC §112, second paragraph and 35 USC §102(b).

II. Rejections Under 35 USC §101 and §112, First Paragraph

Claims 19 and 62 stand rejected under §101 and §112, first paragraph as allegedly inoperative, therefore lacking in patentable utility, and as nonenabling. Applicants respectfully traverse the rejection.

As applicants have maintained throughout the prosecution, UTAA compositions and methods for their use have been shown to be effective at eliciting an immune response in patients with melanoma. In many patients, this response is capable of inhibiting the proliferation of melanoma tumors and, in some cases, even causing tumor regression. Applicants again point to the article by Morton *et al.* in *Annals of Surgery* (1992) as providing evidence that UTAA would function as an anti-cancer vaccine *in vivo*. Thus, the examiner's statement that "[t]he

specification does not set forth any data or experimental results" is misleading given other evidence of record.

Nonetheless, it is applicants' position that proof of therapeutic efficacy is not required in this case for satisfaction of the utility requirement of §101 and the enablement requirement of §112, first paragraph. As set forth in the specification, UTAA is useful as an immunogen for generating anti-UTAA antibodies. For example, the preparation of diagnostic antibodies is disclosed in the specification at page 23, line 7-10; page 28, line 29, to page 29, line 28; page 36, line 25, to page 37, line 7; and page 41, line 28, to page 44, line 11.

Moreover, the diagnostic utility of the subsequent anti-UTAA antibody is demonstrated in the specification. Example IX (pages 31-32) demonstrates preparation and carrying out of an assay for UTAA. Example XXVIII (pages 49-50) demonstrates the detection of UTAA in the urine of cancer patients -- only 2% false positives with almost 70% known positives identified. Lastly, Example XXIX (pages 50-51) demonstrates a relationship between UTAA and recurrence in the urine of cancer patients. All of the foregoing support the use of UTAA as an immunogen in the preparation of diagnostic antibodies.

It should be pointed out that in the Office Action mailed on December 1, 1993, the previous examiner distinguished the term

vaccine, allegedly defined by Webster's New World Dictionary, 3rd College Edition, as "to produce immunity to a specific disease." Based on this definition, the previous examiner noted that "vaccines are not used to raise antibodies useful for diagnosis," and suggested that applicants either abandon the vaccine language in the claims or revise the definition of vaccine. Applicants chose the former suggestion, removing the vaccine language and introducing the more expansive term "antigen composition" at the behest of the examiner. While a vaccine clearly would be included within the an "antigen composition," so too would a substance intended simply to elicit antibodies. Thus, as analyzed by the previous examiner, the present claims are properly drawn to compositions for use in the production of antibodies, thereby permitting applicants' reliance on a diagnostic utility.

The new examiner has rejected applicants' submission regarding a diagnostic utility for UTAA (claim 62) and methods involving the administration of UTAA to a subject (claim 19), however. Although the examiner admits that the recitations of claim 19 are sufficient to describe a method leading to the production of anti-UTAA antibodies, the examiner concludes "that the ultimate purpose of the induction of antibody by this method, is to cause some type of response in the subject with respect to

the tumor cells present."[1] The examiner goes on to state that "typical methodology" for the production of monoclonal antibodies is by hybridoma production. Finally, the examiner turns to statements in the specification regarding vaccine efficacy and again concludes that "the ultimate 'utility' of the compositions and resultant antibodies are to effect *in vivo* treatment of cancer."

Applicants respectfully submit that the examiner's comments with regard to the "ultimate" use or utility of applicants' invention are legally without relevance. Where an invention is disclosed as having more than one use, the case law is clear in requiring that only a single utility be established, and enabled, to meet the requirements of §101 and §112. This utility need not be the most commercially-relevant utility, the most obvious utility or the "ultimate" utility. So long as **ANY** of the disclosed and enabled utilities fulfills the requirements of §101 and §112, first paragraph, a claim to that invention passes statutory muster.

As stated in *Carl Zeiss Stiftung v. Renishaw plc*, 20 USPQ2d 1094, 1100 (Fed. Cir. 1991),

> An invention need not be the best or the only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he

[1] Claim 19, prior to amendment, recited "the production of antibodies reactive with tumor cells in the subject...."

> fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility."

This quotation is particularly relevant here with respect to the examiner's comments regarding (i) "typical methodology" for hybridoma production and (ii) production of antibodies in a subject that are reactive with tumor cells in that subject. Applicants emphasize that even though a given claim might recite a non-preferred or atypical use, that fact alone cannot undermine utility of the claim so long as the use is operable and enabled.

Another example where "ultimate" use was found to be irrelevant was *Ex parte Alt*, 162 USPQ 127 (POBA 1968). There, the Board held that the fact that ingredients used in a claimed method were too expensive to permit commercialization did not establish lack of utility. Rather, <u>any</u> degree of utility has been held sufficient to support a patent. *In re Nelson*, 126 USPQ 242 (CCPA 1960). It is not the <u>extent</u> of the utility that governs but the existence of <u>some</u> utility; utility is established even if only partial success is attained or as long as some useful information is achieved using claimed assay. *Emery Industries, Inc. v. Schumann*, 45 USPQ 12 (7th Cir. 1940).

Applicants also wish make two subsidiary points. First, the examiner's comments appear directed solely at claim 19 which, prior to amendment herein, contained the recitation of "production of antibodies reactive with tumor cells in the

subject." The examiner has offered no explicit reasoning to support a rejection for lack of utility/enablement of a composition according to claim 62. Second, applicants note the proposed amendment of claim 19 to remove the recitation "reactive with tumor cells in the subject." Thus, the claim now recites production of antibodies to UTAA upon administration of a composition according to claim 62. This amendment is designed only to clarify the claim, and applicants emphasize that the induction or enhancement of antibodies in a subject with tumor cells, as recited originally, remains within the scope of the claim.

In light of the foregoing discussion, applicants submit that the rejection under §101 and §112, first paragraph is improper and respectfully request reconsideration and withdrawal thereof.

III. Rejections Under 35 USC §112, Second Paragraph

Claim 19 stands rejected under §112, second paragraph as allegedly indefinite. The rejection is based on the fact that claim 19 depends from claim 47, claim 47 being a non-elected species. Applicants traverse the rejection as claim 47 has not been canceled but merely has been withdrawn from consideration. Claims may properly depend from any pending claim, whether or not they have been withdrawn from consideration. In order to advance the prosecution, however, applicants have amended claim 19 to depend from claim 62.

IV. Rejections Under 35 USC §102(b)

Claims 19 and 62 stand rejected under §102(b) as allegedly anticipated by Gupta *et al.* (1987) (abstract). Gupta is said to disclose vaccination of melanoma patients with the tumor cell line designated M14 and that this cell line "inherently" produces UTAA. Key to the rejection is the examiner's allegation that, here, "the claim language fails to exclude the entire cell." Applicants respectfully traverse the rejection.

A careful review of the claim language is in order and, therefore, both pending claims are reproduced below:

> 19. A method for inducing or enhancing in a subject the production of antibodies reactive with UTAA comprising administering an effective amount of the antigen composition of claim 62.
>
> 62. An antigen composition comprising a purified tumor antigen, wherein the tumor antigen is identified as comprising Urinary Tumor Associated Antigen (UTAA) subunit which, after reduction by ß-mercaptoethanol and separation by SDS-polyacrylamide gel electrophoresis, exhibits a molecular weight of about 90 to 100 kD.

Applicants point out that claim 62 recites "a purified tumor antigen ... (UTAA) subunit." Claim 19 depends from claim 62 and, therefore, also includes the recitation of "a purified tumor antigen ... (UTAA) subunit."

As stated above, the rejection apparently derives from the examiner's belief that the Gupta abstract inherently discloses UTAA-producing cell line, designated M14. This, coupled with the

failure of applicants to exclude a whole cell line from the claim, gives rise to the alleged anticipation. It should be noted, however, that applicants do not claim a UTAA-producing cell line but, instead claim an antigen composition comprising a purified UTAA subunit. Clearly, even if one were to accept the examiner's position that M14 produces UTAA, there is nothing in the abstract from which it could be inferred that UTAA was available in a purified form.

In making a comparison of the claimed invention with the prior art, it is necessary to look at each and every recitation of the claims. "Rejections under 35 USC §102 are proper only when the claimed subject matter is identically disclosed or described in the prior art. *In re Arkley*, ...172 USPQ 524 ([CCPA] 1972). In other words, to constitute anticipation, all material elements recited in a claim must be found in one unit of the prior art. *Soundscriber Corp. v. United States*, ...148 USPQ 298 (Ct.Cl. 1966)." *In re Marshall*, 198 USPQ 344 (CCPA 1978). Because the reference fails to disclose, inherently or otherwise, a purified UTAA, a rejection claims 19 and 62 as anticipated cannot stand.[2]

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[2] Applicants have provided two new claims, claims 63 and 64, that recite particular aspects of purifity. Claim 63 recites 100-fold purification for UTAA subunit (specification at page 18, lines 18-19) and claim 64 recites a 0.6% protein concentration for UTAA subunit (specification at page 23, lines 16-18).

Even if the claims were not so limited, they could not be held inherently anticipated by Gupta. First, with respect to claim 62, applicants point out that the inherency doctrine does not apply to situations where the claimed product was produced undetected in minuscule amounts. *In re Seaborg*, 140 USPQ 659 (CCPA 1964). Applicants submit that UTAA was not detected by Gupta and that the overall amounts produced would have to be considered minuscule.

Second, with respect to claim 19, applicants note that inherency cannot be based on a prior art process when those of skill in the art did not realize the result of the process. *In re Marshall*, 198 USPQ 344 (CCPA 1978); *In re Fenton*, 179 USPQ 295 (CCPA 1973). Since Gupta had not purified UTAA or identified a subunit thereof, it would have been impossible to predict a method of immunization as recited.

Nor may an obviousness rejection be contemplated given the foregoing facts. The fact that a result might flow inherently from the prior art is immaterial if the skilled artisan "would not appreciate or recognize that inherent result." *In re Naylor*, 152 USPQ 106 (CCPA 1966). Citing *In re Spormann*, 150 USPQ 449 (CCPA 1966), the *Naylor* court went on to state that

> [t]he inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. **Obviousness cannot be predicated on what is unknown**.

Id. at page 452 (emphasis added). Here, the fact that culturing M14 cells might have produced UTAA prior to the present invention is absolutely irrelevant. Those of skill in the art could not be motivated further to purify a UTAA subunit as claimed because it had yet to be identified. Without motivation, there can be no *prima facie* case and no rejection.

Because both claims 19 and 62 recite a purified form of UTAA subunit, and the prior art fails to disclose such a composition, the rejection is improper. Applicants respectfully request that the rejection be reconsidered and withdrawn.

Claims 19 and 62 stand rejected under §102(b) as allegedly anticipated by Real *et al.* (U.S. Patent 4,562,160). Real is said to disclose an antigen composition comprised of a tumor associated antigen having a molecular weight of 90-100 kD which is useful for antibody production. Presumably, the examiner equates UTAA with Real's antigen, designated FD. Applicants respectfully traverse the rejection.

In the response filed on March 31, 1994, applicants noted that Real's disclosure characterized FD as having a non-reduced molecular weight of 90-100 kD, a pI of 5.5 and present in <3% of melanoma lines tested. The corresponding numbers for UTAA -- molecular weight of 590-620 kD, pI of 6.1 and 70-75% prevalence in melanoma lines -- clearly are distinguishable. The examiner

responded by noting (i) that the pI reported for UTAA is 590-620 kD unreduced, but 90-100 kD under reducing conditions, (ii) that applicants' reliance on differences in prevalence was misplaced as one cannot rely on limitations not recited in the claims and (iii) that a difference of 5.5 to 6.1 in isoelectric point was well within experimental error.

As a point of departure, applicants note that the central question here is whether Real's FD is the same as the UTAA subunit now claimed. In resolving this question, it is incumbent upon the examiner to consider all the evidence presented in coming to a conclusion that FD and UTAA subunit are or are not the same. For the following reasons, applicants submit that the record is sufficient to

First, the examiner is quite correct in noting that UTAA, under reducing conditions, runs at about 90-100 kD in PAGE. Nonetheless, it also is true that UTAA holoantigen runs at 590-620 kD under non-reducing conditions. Given these figures, what can be said regarding the molecular weight of Real's FD? As the examiner likely has observed, Real notes that FD runs at 90 kD on PAGE (column 4, line 59; column 5, line 8). It is important to note that at column 3, lines 12-15, Real describes the treatment of "unreduced samples." The only reasonable inference one can draw, reading the reference as a whole, is (i) that both reducing

and non-reducing gels were run and (ii) that under either analysis, FD ran at 90 kD.

Turning to the question of prevalence on melanoma cells lines, applicants concede the veracity of the examiner's abstract statement that one cannot rely on limitations not recited in the claims to distinguish over the prior art. That, however, is not the situation at hand. Claim 62 recites "Urinary Tumor Associated Antigen (UTAA)." This term is defined by the specification, for example, at pages 32-33, where it is reported that sera from 63% of disease-bearing melanoma patients showed reactivity with UTAA. In another test for anti-UTAA activity, described at pages 58-60, it was shown that some 37% of patients had sera which recognized UTAA. It now has been confirmed that 70-75% of melanoma cell lines express UTAA. When compared with the prevalence of FD on melanoma cells (<3%), it is clear that UTAA, as defined in the specification, is not the same as FD.

Taken separately, the showing regarding the difference in molecular or the difference in prevalence on melanoma cells would be sufficient to rebut the examiner's allegation of anticipation. Taken together, there should be no question that the present invention is distinguishable from that disclosed by Real.

Finally, applicants note the examiner's statement that a difference of 5.5 to 6.1 in isoelectric point determinations is

with standard error. Applicants traverse this assertion and hereby call for an affidavit under 37 CFR §1.107(b) supporting the above-referenced isoelectric point equivalence and reserve the right to challenge the affidavit with evidence to the contrary. See *In re Ahlert*, 165 USPQ 421 (CCPA 1970) ("Assertions of technical facts in areas of esoteric technology must always be supported by citation to some reference work recognized as standard in the pertinent art .... Allegations concerning specific 'knowledge' of the prior art, which might be peculiar to a particular art should also be supported....").

In summary, the evidence of record does not support the conclusion that UTAA, in either its non-reduced or reduced forms, is the same as Real's FD. Thus, applicants submit that the rejection is improper and request reconsideration and withdrawal thereof.

V. Summary

In light of the foregoing amendments and remarks, applicants submit that all claims are in condition for allowance and solicit an early indication to that effect. Should Examiner Sidberry feel that further discussion of any remaining issues would advance the prosecution, she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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